

# Skin-related symptoms following exposure to recreational water: a systematic review and meta-analysis

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**Abstract** Exposure to contaminated recreational waters (defined by levels of fecal and other types of indicator bacteria) is associated with adverse health outcomes. The principal health outcome studied previously has been gastrointestinal illness. Although many studies included reports of frequent skin complaints (e.g. rash or itch) following recreational water exposure, no systematic reviews have examined the association between indicator levels and skin-related symptoms. Twenty relevant peer-reviewed studies were identified. The relative risks (swimmers vs. non-swimmers) of skin-related symptoms among those exposed to recreational water with bacterial indicator concentrations above threshold levels were determined using meta-analysis. Similarly, the relative risks (swimmers vs. non-swimmers) of skin-related complaints after exposure to water with bacterial indicator concentrations below threshold levels were determined. The ratio of these odds ratios (ROR) was then computed for each indicator. The risk of skin-related symptoms was significantly elevated in marine water with high levels of total coliforms ROR 1.86, (95% CI 1.21, 2.87); fe-

cal coliforms ROR 1.45 (95% CI 1.02, 2.07); *E. coli* ROR 1.98, (95% CI 1.43, 2.75); enterococci ROR 2.04 (95% CI 1.34, 3.09) and fecal streptococci ROR 1.70 (95% CI 1.07, 2.71). However, no significant associations with water quality indicators were demonstrated for the freshwater indicators examined (total coliform, fecal coliform, *E. coli*). Swimmers exposed to marine water at high levels of several indicator bacteria experience a significant increase in skin-related symptoms compared to non-swimmers. This relationship was not demonstrated in freshwater settings.

**Keywords** Recreational water · Bacterial indicators · Rash · Skin disease · Marine water · Fresh water

## Introduction

Health hazards associated with recreational water exposure have been a subject of study since the 1950s. In response to these concerns, the U.S. Environmental Protection Agency published guidelines for ambient water quality (U.S. EPA 1986). These guidelines recommended that for marine waters the geometric means of at least five samples taken over a 30 day period should not exceed 35 colony forming units of enterococcus per 100 mL. For fresh recreational waters, the cut-off points were 33 colony forming units (cfu) of enterococcus per 100 mL, and 126 cfu of *E. coli* per 100 mL (U.S. EPA 1986; Wade et al. 2003).

These recommendations were based on associations between fecal indicator bacteria and gastrointestinal illnesses. Gastrointestinal illness, however, may not be the only adverse health outcome associated with exposure to recreational waters. Skin, respiratory, ear, and other ailments are potentially associated with exposure to contaminated waters (WHO 2001). Although several studies have included an

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examination of the association between recreational water exposure and skin outcomes, no previous review has summarized the evidence systematically. The primary goal of this investigation is to quantify the association between microbial indicators used to monitor recreational water quality and skin-related outcomes in non-outbreak conditions in both marine and freshwater settings.

## Methods

### Literature search

The literature search was done using five electronic databases: PUBMED (<http://www.ncbi.nlm.nih.gov/pubmed/>), BIOSIS (<http://apps.isiknowledge.com/>), Web of Science (<http://apps.isiknowledge.com/>), EMBASE (<http://openaccess.dialog.com/med/>), and ProQuest Dissertation and Theses (<http://proquest.umi.com/pqdweb>) for all dates until August 2008. The search terms used included key words “water and health,” “water and fecal,” “water and feces,” “water and indicator,” “recreational water and health,” as well as permutations of the above keywords. We also contacted experts in the field and reviewed the citations of relevant studies for other relevant studies.

After gathering all available studies, we reviewed the titles and abstracts and retained relevant ones for full-text review. Studies were retained if the abstract and title pertained to health effects with respect to swimming in fresh or salt waters, and if the abstract or title suggested that microbiological quality of the water was measured. Studies published in all languages were considered, as long as the title and abstract were available in English.

### Selection criteria

Studies were included in this review if they met the following criteria:

**Water exposure:** Studies related to marine (ocean) or fresh (lakes, rivers) waters were included, but studies involving swimming pools and other treated bodies of water were excluded. All forms of water contact were included (swimming, sporting events, bathing, etc.).

**Water quality measures:** Studies had to include at least one numeric measure of the microbiologic quality of the water. Studies without quantitative measures of microbiologic water quality were excluded.

**Health outcomes:** In addition to a measure of microbial water quality, a measure of human health associated with microbial water quality had to be reported. After full-text review, if no measure of skin-related symptoms (irritation, rash, infection, itchiness, etc.) was reported, the study was excluded.

**Study design:** Because the purpose of this review was to determine the relationship between microbial indicators and skin-related outcomes under non-outbreak conditions, only studies that dealt with endemic situations were considered for this review. Studies were also required to report data on a control group (otherwise we could not calculate a measure of relative risk).

**Study characteristics:** If a publication was based on data that had been previously published, the most recent analysis was abstracted and the earlier publication was excluded. Also, only peer-reviewed publications were retained.

### Data abstraction

The data were abstracted independently by two authors (C.K.d. and V.Y.). For each study, the following data were abstracted: microbial water quality measure (type and numerical value), water type (marine or fresh), population studied, geographic location, study size, study design, how skin symptoms were defined, covariates adjusted for, comparison group, information on swimming exposure (type and duration), relative risks, and confidence bounds. If a measure of relative risk was not reported, then data were abstracted and used to calculate the odds ratio and its 95% confidence interval. If a publication reported data from several study sites, or the same site over several years, data for each site were abstracted and treated as a separate study (Table 2). If a study did not report a measure of relative risk comparing swimmers to a non-swimmer comparison group, but did have a different comparison group (i.e., swimmers in waters with minimal contamination; Haile et al. 1999), those relative risks were extracted instead. Three indicators (total fungi, *Candida*, and enteroviruses) were excluded from analysis because too few studies (< 2) examined their relation to skin-related outcomes.

A total of eight microbial indicators were included as part of the marine water meta-analysis and six as part of the freshwater meta-analysis (Table 2). The indicators included in the marine water analysis were total coliform, fecal coliform, fecal streptococci, *E. coli*, enterococci, *Klebsiella*, *P. aeruginosa*, and staphylococci. For the freshwater analysis, total coliform, fecal coliform, fecal streptococci, *E. coli*, enterococci, and staphylococci were included. Indicators were selected for analysis if two or more studies examined the indicators in relation to skin-related outcomes. Even though some indicators are currently recommended for use (i.e., U.S. EPA recommends enterococci and *E. coli* for fresh waters) this is based on their association with gastrointestinal illnesses (Cabelli 1983), not other symptoms. Thus, both currently recommended indicators and indicators not in current use were included.

### Cut-off points for threshold values

Values to define high bacterial levels were obtained for total coliforms, fecal coliforms, fecal streptococci, and enterococci, and these cut-off points were analyzed to determine if there was an association between these levels and skin-related health outcomes. The California State Water Resources Control Board (1990) recommended that a cut-off point of 10,000 cfu / 100 mL be used for total coliform in marine waters, as well as a cut-off point of 400 cfu / 100 mL for fecal coliforms (California State Water Resources Control Board 1990b). Haile et al. (1999) recommended a cut-off point of 35 cfu / 100 mL for *E. coli*. Ogan (1994) recommended a cut-off point of 35 cfu / 100 mL for fecal streptococci, and the EPA recommendation for a cut-off point using enterococci was 35 cfu / 100 mL (U.S. EPA 1986). California cut-off points were not selected preferentially; rather, any cut-off points found were considered. Alternative cut-off points were not found, potentially because non-recommended indicators are not as well researched.

For freshwater indicators, cut-off points were also obtained from the literature. The California Department of Public Health (2000) recommended a fecal coliform cut-off point of 200 cfu / 100 mL. A cut-off point of 1,000 cfu / 100 mL was recommended by the San Diego Water Board (2007) for total coliform. For fecal streptococci, a cut-off point of 100 cfu / 100 mL was recommended in Wiedenmann et al. (2006); however, no studies were identified with fecal streptococci levels higher than this cut-off, so no comparison could be made.

Cut-off points proposed by the EPA and WHO were chosen preferentially, but when there were no established guidelines, cut-off points recommended by the literature were used instead, due to convenience. In marine settings, the EPA provided a recommended cut-off point for enterococci, but for the remaining fresh and marine indicators, there were no WHO or EPA recommended values. No cut-off points were found at all for concentrations of *Klebsiella*, *P. aeruginosa*, or staphylococci in marine waters, and no recommended cut-off point was found for staphylococci concentrations in fresh waters. Thus, no ROR was calculated, and only odds ratios comparing swimmers to control groups were computed for these indicators through meta-analysis.

### Data analysis

Separate analyses were used to examine each combination of microbial indicator and water type (marine and fresh). If a study reported microbial indicator values over a range, the median value of that range was used in our analyses. Exposure categories were formed by basing defining thresholds for high exposure based on cut-off points listed in U.S. EPA and WHO criteria or guidelines recommended for safe recreational water (U.S. EPA 1986;

WHO 2001), and if those were unavailable, cut-off points recommended by the literature were used (San Diego Water Board 2007; Haile et al. 1999; California Department of Public Health 2000; Wiedenmann et al. 2006; Ogan 1994; Wade et al. 2003).

If a study reported multiple relative risks from a single study site, the highest exposure measure and its relative risk was used for analysis, consistent with the prior work of Wade et al. (2003). This prevented a single study from receiving more weight solely because of the number of results presented. However, if a study reported findings from multiple, independent study sites, the microbial indicator level and relative risk from each study site was recorded and used for analysis. Also, if a certain beach was studied one year and then studied again on a subsequent year, those study results were recorded separately. One potential concern related to treating each site in a report as a separate observation lies in the fact that the findings from those sites might, theoretically, not be independent of each other. However, pooling such sites might not be appropriate either because of differences in the swimming populations that utilized those beaches and in the indicator levels that were present at the time. Rather than combining potentially different populations and sites, we analyzed them as separate observations (Table 2).

### Meta-analysis of study site results

We calculated a summary relative risk of skin-related outcomes for each microbial indicator level (i.e., one odds ratio for swimmers vs. non-swimmers above the indicator cut-off point and one odds ratio for swimmers vs. non-swimmers below the cut-off point using fixed-effects models if no heterogeneity was present; otherwise, random-effects models were utilized). Heterogeneity of study results was assessed for each analysis using the Q statistic (DerSimonian and Laird 1986).

A binary variable was created to categorize the data into the sites with mean indicator levels below the cut-off point and those above. We then compared the odds ratio of skin-related outcomes for exposure above the cut-off point to the odds ratio of skin-related outcomes below the cut-off point. The mean difference between the log relative risks was taken, and the null hypothesis being tested was that the difference was equal to zero. The difference was then exponentiated to create the ratio of odds ratios (ROR). A ROR above 1.0 suggests an increased risk of skin-related symptoms among those exposed to indicator levels above the cut-off as compared to those exposed to indicator levels below the cut-off point (Altman and Bland 2003). For example, if the OR for swimmers vs. non-swimmers was 5.0 above the indicator cut-off point and 2.0 below the cut-off point, then the ROR would be reported as 2.5 (= 5.0/2.0).

## Heterogeneity

Sources of heterogeneity that might explain the variability between the results of different studies were investigated by using a random-effects meta-regression model (Thompson and Sharp 1999). The outcome being modeled was the natural log of the relative risk for skin-related outcomes and predictor variables were indicator variables for whether or not a study adjusted for a particular covariate (available covariates were: gender, respondent, socioeconomic status, age, health or allergy history, visitor or native status, ethnicity, food consumption, knowledge of beach health hazards, place of residence, marital status, use of randomization, exposure activity at the beach, insect repellent use, sunblock use, physical weather and wave data, beach density, presence of animals or boats, and swimming history), study size, study type, and geographic location of the study. The final model was chosen by excluding covariates with  $p$ -values  $> 0.2$ .

Analyses were performed using Stata 10.0 for the Macintosh (Stata Corporation 2007).

## Results

A total of 3,468 titles and abstracts were reviewed for relevance, and 47 of these were retained for full text review. Of these, 20 studies (Table 1) were retained for final analysis.

Twenty-seven studies were excluded because three studies included no information or inadequate information on microbiological water quality (Amson 1991; New Jersey DoH 1988; Baylet and Sinegre 1984), 16 were excluded because skin outcome data was not reported or was not adequately reported (Balarajan et al. 1991; Bandaranayake et al. 1995; Bonilla et al. 2007; Cheung et al. 1991; Dufour 1984; Fattal et al. 1987; Fleisher et al. 1996; Harrington et al. 1993; Kocasoy 1989; McBride et al. 1998; Philipp et al. 1985; Seyfried et al. 1985b; Wiedenmann et al. 2006; Foulon et al. 1983; Kueh et al. 1995; Marino et al. 1995), one was excluded because the indicator used was not reported in any other study (Pilotto et al. 1997, cyanobacteria), three were excluded because they did not generate any relevant primary data (Burke 2002; Pruss 1998; Robinton 1966), two were excluded because the same results were published elsewhere (Haile 1996; Zmirou et al. 1990), and one was excluded because data on a control group was not reported (Stevenson 1953).

### Characteristics of included studies

The 20 studies retained for inclusion in the meta-analysis had study populations ranging from 104 to 23,241 individuals. Nine of the 20 studies were conducted in freshwater settings, while the remaining 11 studies were conducted in marine water settings (Table 1). One publication, Cabelli (1983), reported data from two separate studies (one in Louisiana, USA, and one in Egypt).

**Table 1** Final list of studies retained, by date of publication, location of study, marine or freshwater exposure, total study sample size, and study design

| Reference                     | Location     | Water Type | Sample Size | Study Type           |
|-------------------------------|--------------|------------|-------------|----------------------|
| Cabelli et al. (1979)         | USA          | Marine     | 8073        | Prospective Cohort   |
| Cabelli (1983)                | USA/Egypt    | Marine     | 3778/23241  | Prospective Cohort   |
| Seyfried et al. (1985)        | Canada       | Fresh      | 4537        | Prospective Cohort   |
| Dewailly et al. (1986)        | Canada       | Fresh      | 120         | Prospective Cohort   |
| Ferley et al. (1989)          | France       | Fresh      | 5737        | Retrospective Cohort |
| Cheung et al. (1990)          | Hong Kong    | Marine     | 18741       | Prospective Cohort   |
| Jones et al. (1991)           | UK           | Marine     | 276         | Randomized Cohort    |
| Alexander et al. (1992)       | UK           | Marine     | 703         | Prospective Cohort   |
| Fewtrell et al. (1992)        | UK           | Fresh      | 516         | Prospective Cohort   |
| Von Schirnding et al. (1992)  | South Africa | Marine     | 733         | Prospective Cohort   |
| Charoencra and Fujioka (1995) | USA          | Marine     | 106         | Case-Control         |
| Medema et al. (1995)          | Netherlands  | Fresh      | 395         | Prospective Cohort   |
| Van Asperen et al. (1997)     | Netherlands  | Fresh      | 104         | Randomized Cohort    |
| Haile et al. (1999)           | USA          | Marine     | 10459       | Prospective Cohort   |
| Prieto et al. (2001)          | Spain        | Marine     | 1858        | Prospective Cohort   |
| Lee et al. (2002)             | Indonesia    | Fresh      | 435         | Cross-Sectional      |
| Dwight et al. (2004)          | USA          | Marine     | 1873        | Cross-Sectional      |
| Wiedenmann et al. (2006)      | Germany      | Fresh      | 1759        | Randomized Cohort    |
| Colford et al. (2007)         | USA          | Marine     | 8797        | Prospective Cohort   |
| Wade et al. (2008)            | USA          | Fresh      | 21015       | Prospective Cohort   |

**Table 2** Six freshwater indicators and 8 marine indicators retained for final analysis. Studies indicate the number of publications dealing with that indicator and skin disease, and sites refer to the number of beaches/independent locations that were studied in those publications

| Freshwater Indicators | Studies | Sites | Authors/Sites*   |
|-----------------------|---------|-------|--|
| Fecal Coliform        | 6       | 3     | Ferley et al. (1989)—3 Sites<br>Lee et al. (2002)—1 Site<br>Dewailly et al. (1986)—1 Site<br>Fewtrell et al. (1992)—2 Sites<br>Medema et al. (1995)—1 Site<br>Seyfried et al. (1985)—1 Site                                |
| Total Coliform        | 2       | 4     | Ferley et al. (1989)—3 Sites<br>Lee et al. (2002)—1 Site   |
| Fecal Streptococci    | 4       | 7     | Ferley et al. (1989)—3 Sites<br>Fewtrell et al. (1992)—2 Sites<br>Medema et al. (1995)—1 Site<br>Seyfried et al. (1985)—1 Site   |
| <i>E. coli</i>        | 3       | 3     | Medema et al. (1995)—1 Site<br>Van Asperen et al. (1997)—1 Site<br>Wiedenmann et al. (2006)—1 Site   |
| Enterococcus          | 3       | 3     | Wade et al. (2008)—1 Site<br>Van Asperen et al. (1997)—1 Site<br>Wiedenmann et al. (2006)—1 Site   |
| Staphylococci         | 3       | 4     | Fewtrell et al. (1992)—2 Sites<br>Sevfr ed et al. (1985)—1 Site<br>Van Asperen et al. (1997)—1 Site  |
| Marine Indicators     | Studies | Sites | Authors/Sites*   |
| Enterococci           | 6       | 25    | Cheung et al. (1990)—9 Sites<br>Cabelli et al. (1979)—2 Sites<br>Cabelli (1983)—10 Sites<br>Haile et al. (1999)—1 Site<br>Colford et al. (2007)—1 Site<br>Von Schirnding et al. (1992)—2 Sites                             |
| <i>E. coli</i>        | 4       | 22    | Cheung et al. (1990)—9 Sites<br>Cabelli et al. (1979)—2 Sites<br>Cabelli (1983)—10 Sites<br>Haile et al. (1999)—1 Site   |
| Total Coliforms       | 7       | 9     | Prieto et al. (2001)—1 Site<br>Jones et al. (1991)—1 Site<br>Cabelli et al. (1979)—2 Sites<br>Alexander et al. (1992)—1 Site<br>Haile et al. (1999)—1 Site<br>Colford et al. (2007)—1 Site<br>Dwight et al. (2004)—2 Sites |
| Fecal Streptococci    | 5       | 14    | Cheung et al. (1990)—9 Sites<br>Prieto et al. (2001)—1 Site<br>Jones et al. (1991)—1 Site<br>Cabelli et al. (1979)—2 Sites<br>Alexander et al. (1992)—1 Site   |

\*Only distinct beaches or sites that were analyzed separately and for which a separate relative risk was reported were counted as a site



**Table 2** (Continued)

| Marine Indicators    | Studies | Sites | Authors/Sites*   |
|----------------------|---------|-------|--|
| Fecal Coliform       | 8       | 18    | Cheung et al. (1990)—9 Sites<br>Prieto et al. (2001)—1 Site<br>Jones et al. (1991)—1 Site<br>Cabelli et al. (1979)—2 Sites<br>Alexander et al. (1992)—1 Site<br>Haile et al. (1999)—1 Site<br>Colford et al. (2007)—1 Site<br>Von Schirnding et al. (1992)—2 Sites |
| Klebsiella           | 2       | 11    | Cheung et al. (1990)—9 Sites<br>Cabelli et al. (1979)—2 Sites  |
| <i>P. aeruginosa</i> | 4       | 13    | Cheung et al. (1990)—9 Sites<br>Prieto et al. (2001)—1 Site<br>Jones et al. (1991)—1 Site<br>Cabelli et al. (1979)—2 Sites   |
| Staphylococci        | 3       | 11    | Cheung et al. (1990)—9 Sites<br>Prieto et al. (2001)—1 Site<br>Charoencra and Fujioka (1995)—1 Site  |

\*Only distinct beaches or sites that were analyzed separately and for which a separate relative risk was reported were counted as a site

### Study design

There were five different types of studies represented in the sample of 20 included studies: three randomized controlled trials, two cross-sectional studies, one retrospective cohort study, one case-control study, and 13 prospective cohort studies.

Ten of the prospective cohort studies were traditional cohort studies (Cabelli et al. 1979; Cabelli 1983; Cheung et al. 1990; Haile et al. 1999; Prieto et al. 2001; Seyfried et al. 1985; Von Schirnding et al. 1992; Colford et al. 2007; Wade et al. 2008; Alexander et al. 1992). These studies recruited individuals on the beach and collected information on their water exposure that day. Follow-up of these individuals for skin-related illness was conducted 3 to 35 days after exposure. At least one water sample was collected on the day of exposure. In all but one study, swimmers were compared to non-swimmers with respect to skin-related illnesses. Haile et al. (1999) instead compared swimmers in waters with higher levels of contamination to swimmers in waters with minimal levels of contamination.

The remaining three prospective cohort studies (Dewailly et al. 1986; Fewtrell et al. 1992; Medema et al. 1995) were conducted in the context of an athletic event. Exposed individuals were athletic event participants (triathletes, canoeists, and surfers) while non-swimmers were individuals present at the same event who had no water exposure (employees, etc.). Water samples were collected during the event, and follow-up for skin-related symptoms occurred 5–9 days after the events.

Lee et al. (2002) was one of the cross-sectional studies conducted, and water sampling, current skin-related illness

status, and history of river exposure was collected on the same day. The comparison groups were those with exposure to highly contaminated water vs. lower water contamination. For Dwight et al. (2004), surfers who surfed at least once a week were interviewed at two different beaches (one highly contaminated and one less contaminated) and were asked about symptoms in the past 3 months as well as exposure history for that time. Mean monthly indicator levels were provided by local health agencies.

With respect to randomized trials, Jones et al. (1991) randomly assigned individuals to swimming or non-swimming behavior. Skin-related symptoms were assessed 3 days and 3 weeks after exposure, and water quality was assessed the day of exposure. Van Asperen et al. (1997) also randomized individuals to swimming or non-swimming and assessed skin symptoms one week after exposure. Water quality was measured five minutes before exposure. Wiedenmann et al. (2006) was similar to both of the above: outcomes were measured one week after the study, and individuals were randomized to exposure or non-exposure.

One retrospective cohort study conducted by Ferley et al. (1989) collected data on health status and water exposure the week before. Water quality was assessed by collecting samples in advance of the health surveys. Samples were collected 2 days per week, and the concentrations measured on those days were extrapolated to the adjacent days.

The case-control study conducted by Charoencra and Fujioka (1995) measured water quality at various beaches and then enrolled patients with staphylococcal skin infections and determined their seawater contact 10 days before.

Eleven studies recruited both adults and children (Cabelli et al. 1979; Cabelli 1983; Seyfried et al. 1985; Fer-

**Table 3** Exposure, outcome definitions, and outcome assessment methods for each study included in the meta-analysis. For some studies, limited information was available about outcome assessment methods

| Freshwater Studies           | Exposure Definition                                   | Outcome Definition  | Outcome Assessment   |
|------------------------------|---|---|--|
| Seyfried et al. (1985)       | Any contact   | Skin rash, welts, boils   | Self-report symptoms, telephone interview 7–10 days after, questionnaire mailed if no contact                |
| Dewailly et al. (1986)       | Windsurfers   | Infectious and allergenic skin conditions   | Self-report symptoms, questionnaire 2 days after   |
| Ferley et al. (1989)         | Bathing   | Skin infections   | Self-report symptoms, interviewed 1 week after   |
| Fewtrell et al. (1992)       | Canoeists   | Undefined skin symptoms   | Self-report symptoms, telephone interview 5–7 days after, questionnaire 1 month after                        |
| Medema et al. (1995)         | Triathlon-swim  | Skin or mucosal symptoms  | Self-report symptoms   |
| Van Asperen et al. (1997)    | Head immersion  | Itchy skin, skin rash, present at least 2 parts of the day in the 2 days post trial | Self-report symptoms, questionnaire 5 days after   |
| Lee et al. (2002)            | Daily, some days, never exposure to water             | Doctor inspection for skin conditions   | Doctors assessed symptoms, day of study  |
| Wiedenmann et al. (2006)     | 3 head immersions, 10 minutes in water                | Skin infections or cutereactions  | Doctors assessed symptoms 1 week after, questionnaire 3 weeks after  |
| Wade et al. (2003)           | Waist or higher immersion                             | Rash or itchy skin  | Self-report symptoms, telephone interview 10–12 days after   |
| Marine Studies               | Exposure Definition                                   | Outcome Definition  | Outcome Assessment   |
| Cabelli et al. (1979)        | Head immersion, > 10 min in water                     | Itchy skin, rash, welts   | Self-report symptoms, telephone interview 8–10 days after  |
| Cabelli (1983)               | Head immersion  | Irritations and disturbances of the skin  | US: Self-report symptoms, telephone interview 7–10 days after, Egypt: Self-report symptoms, 1 week follow-up |
| Cheung et al. (1990)         | Head immersion or water touching face                 | Rashes, skin symptoms exclusive of sunburn  | Self-report symptoms, telephone interview 7 days after   |
| Jones et al. (1991)          | Head immersion  | Skin rash   | Self-report symptoms, 3 days after   |
| Alexander et al. (1992)      | Any contact   | Skin rash, itchy skin   | Self-report symptoms, telephone and questionnaire 10 days after  |
| Von Schirnding et al. (1992) | Water contact beyond waist                            | Skin rash, itchy skin, welts  | Self-report symptoms, telephone interview 4 days after   |
| Charoenca and Fujioka (1995) | Seawater contact 10 days before study                 | Staphylococcal skin infections, cultured  | Patients reporting to clinic with skin infections recruited  |
| Haile et al. (1999)          | Head immersion  | Skin rash   | Self-report symptoms, telephone interview 9–14 days after  |
| Prieto et al. (2001)         | Self report swimming activity, no definition reported | Skin irritation, itching  | Self-report symptoms, telephone interview 7 days after   |
| Dwight et al. (2004)         | Surfers in polluted beaches                           | Self reported skin infection  | Self-report symptoms, interview  |
| Colford et al. (2007)        | Head or face under water                              | Skin rashes, infected cuts/scrapes  | Self-report symptoms, telephone interview 14 days after  |

ley et al. 1989; Cheung et al. 1990; Von Schirnding et al. 1992; Haile et al. 1999; Prieto et al. 2001; Colford et al. 2007; Wiedenmann et al. 2006; Wade et al. 2008), while five studies only recruited adults (Jones et al. 1991; Dewailly et al. 1986; Fewtrell et al. 1992; Medema et al. 1995; Dwight et al. 2004). Only four studies focused

only on children (Alexander et al. 1992; Lee et al. 2002; Van Asperen et al. 1997; Charoenca and Fujioka 1995). Definitions of outcomes and exposures for all the included studies are in Table 3.

Most studies used non-swimmers as the comparison group, but the chosen populations differed. Thirteen studies

**Table 4** Additional study information, by freshwater indicator. Water sampling method, laboratory analysis method, suspected contamination source, and comparison groups

| Freshwater Indicator | Study                     | Collection Method   | Lab Method  | Probable Source   | Study Groups   |
|----------------------|---------------------------|---|---|---|--|
| Fecal Coliform       | Ferley et al. (1989)      | 2 × a week at 5 beaches, 30 cm depth                                      | Spread plate or membrane filter procedure with Tergitol and TTC agar, incubated                           | Untreated urban domestic sewage   | Swimmers vs. Non-swimmers                                  |
|                      | Lee et al. (2002)         | Water sampled at survey time  | None Stated   | Pulp Mill, Treated Waste, Point Source  | Village with high pollution vs. Village with low pollution |
|                      | Dewailly et al. (1986)    | One day, 8 sites sampled  | None Stated   | Sewage  | Windsurfers vs. Non-water exposed                          |
|                      | Fewtrell et al. (1992)    | Day of activity   | None Stated   | Several Upstream Sewage Treatment Plants  | Canoeists vs. Non-canoeists                                |
|                      | Medema et al. (1995)      | Samples of 3 sites, 30 cm below surface                                   | Dutch Standard methods  | None Stated   | Swimmers vs. Non-swimmers                                  |
|                      | Seyfried et al. (1985)    | Sample Beaches 2–3 × a day, water and sediment at depth of at least 50 cm | Water: MPN (Most Probable Number) using Standard Methods  | None Stated   | Swimmers vs. Non-swimmers                                  |
| Total Coliform       | Ferley et al. (1989)      | 2 × a week at 5 beaches, 30 cm depth                                      | Spread plate or membrane filter procedure with Tergitol and TTC agar, incubated                           | Untreated urban domestic sewage   | Swimmers vs. Non-swimmers                                  |
|                      | Lee et al. (2002)         | Water sampled at survey time  | None Stated   | Pulp Mill, Treated Waste, Point Source  | Village with high pollution vs. Village with low pollution |
| Fecal Streptococci   | Ferley et al. (1989)      | 2 × a week at 5 beaches, 30 cm depth                                      | Poured plates using D. coccoseal agar   | Untreated urban domestic sewage   | Swimmers vs. Non-Swimmers                                  |
|                      | Fewtrell et al. (1992)    | Day of activity   | None Stated   | Several Upstream Sewage Treatment Plants  | Canoeists vs. Non-canoeists                                |
|                      | Medema et al. (1995)      | Samples of 3 sites, 30 cm below surface                                   | Dutch Standard methods  | None Stated   | Swimmers vs. Non-swimmers                                  |
|                      | Seyfried et al. (1985)    | Sample Beaches 2–3 × a day, water and sediment at depth of at least 50 cm | Water: MPN (Most Probable Number) using Standard Methods, and membrane filter m-Enterococcus agar (Difco) | None Stated   | Swimmers vs. Non-swimmers                                  |
| <i>E. coli</i>       | Medema et al. (1995)      | Samples of 3 sites, 30 cm below surface                                   | Dutch Standard methods  | None Stated   | Swimmers vs. Non-swimmers                                  |
|                      | Van Asperen et al. (1997) | Day of exposure, multiple sites, 250 ml samples                           | Dutch Standard Methods  | Treated sewage  | Primary School children randomized                         |
|                      | Wiedenmann et al. (2006)  | Sampled every 20 min  | MUG Hydrolysis, microtiter plate method   | Treated and untreated municipal sewage, agricultural run-off, waterfowl contamination | Randomized bathers vs. non-bathers                         |



**Table 4** (Continued)

| Freshwater Indicator | Study                     | Collection Method  | Lab Method   | Probable Source   | Study Groups                       |
|----------------------|---------------------------|--|--|---|------------------------------------|
| Enterococcus         | Wade et al. (2008)        | Samples shin and waist deep  | EPA Membrane Filtration Method 1600, and QPCR  | Treated Sewage (Point Source)   | Swimmers vs. Non-swimmers          |
|                      | Van Asperen et al. (1997) | Day of exposure, multiple sites, 250 ml samples                          | Dutch Standard Methods   | Treated sewage  | Primary School children randomized |
|                      | Wiedenmann et al. (2006)  | Sampled every 20 min   | MUD Hydrolysis and formazan formation  | Treated and untreated municipal sewage, agricultural run-off, waterfowl contamination | Randomized bathers vs. non-bathers |
| Staphylococci        | Fewtrell et al. (1992)    | Day of activity  | None Stated  | Several Upstream Sewage Treatment Plants  | Canoeists vs. Non-canoeists        |
|                      | Seyfried et al. (1985)    | Sample Beaches 2–3× a day, water and sediment at depth of at least 50 cm | Water: Gelman Filters, incubated on Vogel-Johnson agar, Sand: Enrich in m-Staphylococcus broth, spread on Vogel-Johnson agar | None Stated   | Swimmers vs. Non-swimmers          |
|                      | Van Asperen et al. (1997) | Day of exposure, multiple sites, 250 ml samples                          | Dutch Standard Methods   | Treated sewage  | Primary School children randomized |

chose to use beach-goers who had no water exposure (Cabelli et al. 1979; Cabelli 1983; Cheung et al. 1990; Prieto et al. 2001; Seyfried et al. 1985; Von Schirnding et al. 1992; Colford et al. 2007; Alexander et al. 1992; Ferley et al. 1989; Jones et al. 1991; Wade et al. 2008; Van Asperen et al. 1997; Wiedenmann et al. 2006), while three studies used employees at a sporting event or athletes with no water exposure at the same sporting venue (Medema et al. 1995; Fewtrell et al. 1992; Dewailly et al. 1986). Haile et al. (1999), Lee et al. (2002), and Dwight et al. (2004) used exposure to less contaminated waters as a comparison group for individuals exposed to highly contaminated waters.

#### Exposure assessment and definitions

If studies did not report direct observation of water exposure, it was assumed that self-report was used instead. For fifteen of the twenty studies, exposure was determined by self-report (Cabelli et al. 1979; Cabelli 1983; Seyfried et al. 1985; Dewailly et al. 1986; Ferley et al. 1989; Cheung et al. 1990; Alexander et al. 1992; Von Schirnding et al. 1992; Haile et al. 1999; Prieto et al. 2001; Lee et al. 2002; Colford et al. 2007; Dwight et al. 2004; Charoenca and Fujioka 1995; Wade et al. 2008). The definition of exposure differed from study to study. The most common definition was head immersion or facial contact (Cabelli et al. 1979; Cabelli 1983; Cheung et al. 1990; Haile et al. 1999; Jones et al. 1991;

Colford et al. 2007). The next most common definition was any contact with the water (Alexander et al. 1992; Seyfried et al. 1985; Von Schirnding et al. 1992; Ferley et al. 1989). Three studies defined exposure as participation in a water-related sporting event (Medema et al. 1995; Fewtrell et al. 1992; Dewailly et al. 1986). See Table 3 for more detailed definitions.

#### Meta-analysis of study site results: marine water

The results of this analysis indicated that for all bacterial indicators tested, the odds ratios (of illness in swimmers vs. non-swimmers) at sites with low indicator levels were significantly smaller than odds ratios at sites with elevated indicator levels. The ROR comparing the odds ratios among swimmers in waters with high concentrations of enterococci vs. the odds ratio among swimmers in water with low concentrations was 2.04 (95% CI 1.34–3.09). For total coliform, the ROR was 1.86 (95% CI 1.21–2.87). Studies with fecal coliform levels above 400 cfu / 100 mL had odds ratios that were 1.45 times larger than studies with lower indicator levels (95% CI 1.02–2.07). For *E. coli*, the ROR was 1.96 (95% CI 1.38–2.79). Studies with elevated fecal streptococci had an elevated odds ratio that was significantly different than a ROR of 1 (ROR = 1.70, 95% CI 1.07–2.71) (Fig. 1).

**Table 5** Additional study information, by marine indicator. Water sampling method, laboratory analysis method, suspected contamination source, and comparison groups

| Marine Indicator | Study                        | Collection Method  | Lab Method  | Probable Source   | Study Groups  |
|------------------|------------------------------|--|---|---|---|
| Enterococci      | Cheung et al. (1990)         | 3 samples per beach, 1 m deep                                | Membrane filtration, incubated on media                     | Human sewage discharge, stormdrains, livestock waste                          | Swimmers vs. non-swimmers   |
|                  | Cabelli et al. (1979)        | Sample several times per day, chest depth 4 in below surface | Membrane filter   | Sewage  | Swimmers vs. Non-swimmers   |
|                  | Cabelli (1983)               | Multiple samples, Chest Depth, just below surface            | Membrane Filter, mE medium                                  | US: None Stated, Egypt: Raw sewage  | Swimmers vs. Non-swimmers   |
|                  | Haile et al. (1999)          | Daily ankle depth samples                                    | Membrane filtration   | Storm Drain Run-off   | Swimmers in more polluted water vs. swimmers in less polluted water |
|                  | Colford et al. (2007)        | Daily, hourly sampling                                       | Membrane Filtration, chromogenic substrate method, and qPCR | Non-point source, human contamination minimal                                 | Swimmers vs. non-swimmers   |
|                  | Von Schirnding et al. (1992) | Day of trial, samples before and during trial                | Standard membrane filtration methods                        | Septic tank overflows, stormwater run-off, fecal contamination in river water | Swimmers vs. Non-swimmers   |
| <i>E. coli</i>   | Cheung et al. (1990)         | 3 samples per beach, 1 m deep                                | Membrane filtration, incubated on media                     | Human sewage discharge, stormdrains, livestock waste                          | Swimmers vs. Non-swimmers   |
|                  | Cabelli et al. (1979)        | Sample several times per day, chest depth 4 in below surface | mC  | Sewage  | Swimmers vs. Non-swimmers   |
|                  | Cabelli (1983)               | Multiple samples, Chest Depth, just below surface            | Membrane Filtration, mTEC medium                            | US: None Stated, Egypt: Raw sewage  | Swimmers vs. Non-swimmers   |
|                  | Haile et al. (1999)          | Daily ankle depth samples                                    | Membrane filtration, Hach Method 10029                      | Storm Drain Run-off   | Swimmers in more polluted water vs. swimmers in less polluted water |

#### Meta-analysis of study site results: fresh water

Analyses of the cut-off points for fecal coliform and total coliform revealed no significant associations. For total coliform, the ROR was 1.17 (95% CI 0.75–1.84). For fecal coliform, the ROR was 1.69 (95% CI 0.88–3.27). The same conclusion was reached with *E. coli* as well (ROR = 0.62, 95% CI 0.03–13.55), though the number of sites included was small ( $n = 3$ ).

#### Meta-analysis of indicators without RORs: marine and fresh water

Three marine indicators (*Klebsiella*, *P. aeruginosa*, and staphylococci) and one freshwater indicator (staphylococci)

had no recommended cut-off point, and so no ROR was calculated. However, a simple regression was used to determine if there was a linear relationship between concentration level of the indicator and the study OR. For *Klebsiella*, the OR associated with a one hundred cfu increase in concentration per 100 mL was 1.16 (95% CI 0.98–1.37). For *P. aeruginosa*, the OR was 1.28 (95% CI 0.30–5.44). For marine staphylococci, the OR was 1.02 (95% CI 0.97–1.06). For freshwater staphylococci, the OR was 1.74 (95% CI 0.17–17.72).

One freshwater indicator, enterococcus, had a recommended cut-off point, but all available studies had indicator concentrations above the cut-off point. For a 100 cfu / 100 mL increase in enterococcus concentrations in freshwa-

**Table 5** (Continued)

| Marine Indicator   | Study                   | Collection Method   | Lab Method   | Probable Source                                      | Study Groups  |
|--------------------|-------------------------|---|--|--|---|
| Total Coliforms    | Prieto et al. (2001)    | 30 cm below surface   | Standard Methods                                     | Sewage Systems                                       | Swimmers vs. Non-Swimmers   |
|                    | Jones et al. (1991)     | Sampled every 20 min at surf, 30 cm, chest depth, and 50 m off-shore. | None Stated  | None Stated  | Bather vs. Non-bather Randomized                                    |
|                    | Cabelli et al. (1979)   | Sample several times per day, chest depth 4 in below surface          | Most Probable Number, mC procedure                   | Sewage   | Swimmers vs. Non-swimmers   |
|                    | Alexander et al. (1992) | 2 samples at waist depth  | Standard Methods                                     | Sewage   | Swimmers vs. Non-swimmers   |
|                    | Haile et al. (1999)     | Daily ankle depth samples   | Membrane Filtration                                  | Storm Drain Run-off                                  | Swimmers in more polluted water vs. swimmers in less polluted water |
|                    | Colford et al. (2007)   | Daily, hourly sampling  | Membrane Filtration and chromogenic substrate method | Non-point source, human contamination minimal        | Swimmers vs. Non-swimmers   |
|                    | Dwight et al. (2004)    | None Stated   | None Stated  | Untreated Urban Run-off (non-point source)           | Polluted vs. Non-polluted beach                                     |
| Fecal Streptococci | Cheung et al. (1990)    | 3 samples per beach, 1 m deep   | Membrane filtration, incubated on media              | Human sewage discharge, stormdrains, livestock waste | Swimmers vs. Non-swimmers   |
|                    | Prieto et al. (2001)    | 30 cm below surface   | Standard Methods                                     | Sewage Systems                                       | Swimmers vs. Non-swimmers   |
|                    | Jones et al. (1991)     | Sampled every 20 min at surf, 30 cm, chest depth, and 50 m off-shore  | None Stated  | None Stated  | Bather vs. Non-bather Randomized                                    |
|                    | Cabelli et al. (1979)   | Sample several times per day, chest depth 4 in below surface          | mSD  | Sewage   | Swimmers vs. Non-swimmers   |
|                    | Alexander et al. (1992) | 2 samples at waist depth  | Standard Methods                                     | Sewage   | Swimmers vs. Non-swimmers   |

ter settings, the OR was 0.88 (95% CI 0.57–1.36). A similar situation occurred with freshwater streptococci, but instead all studies had indicator concentrations lower than the recommended 100 cfu / 100 mL cut-off point. A linear regression was performed, and the OR associated with a 100 cfu / 100 mL increase in concentration was 3.83 (95% CI 0.60–24.39). Linear regression was chosen in lieu of other models mainly because the data were relatively sparse, and thus it was not obvious if the data were clearly linear or non-linear. While more complicated splines and exponential models could have been fit, the interpretation of the coefficients of these models would have been more difficult.

### Heterogeneity

Heterogeneity was detected in several of the analyses ( $p < 0.2$ ), and to explore sources of heterogeneity, meta-regression was used. Factors that were considered were adjustment by the authors for any confounders, or adjustment for a variety of confounders (gender, respondent to survey, socioeconomic status (SES), age, history of health and allergies, visitor or native status, ethnicity, food consumption, knowledge of beach hazards, place of residence, marital status, exposure activities at the beach, insect repellent use, sunblock use, physical and weather data, density of individuals at the beach, presence of boats or animals, and swimming history). These covariates were coded as in-

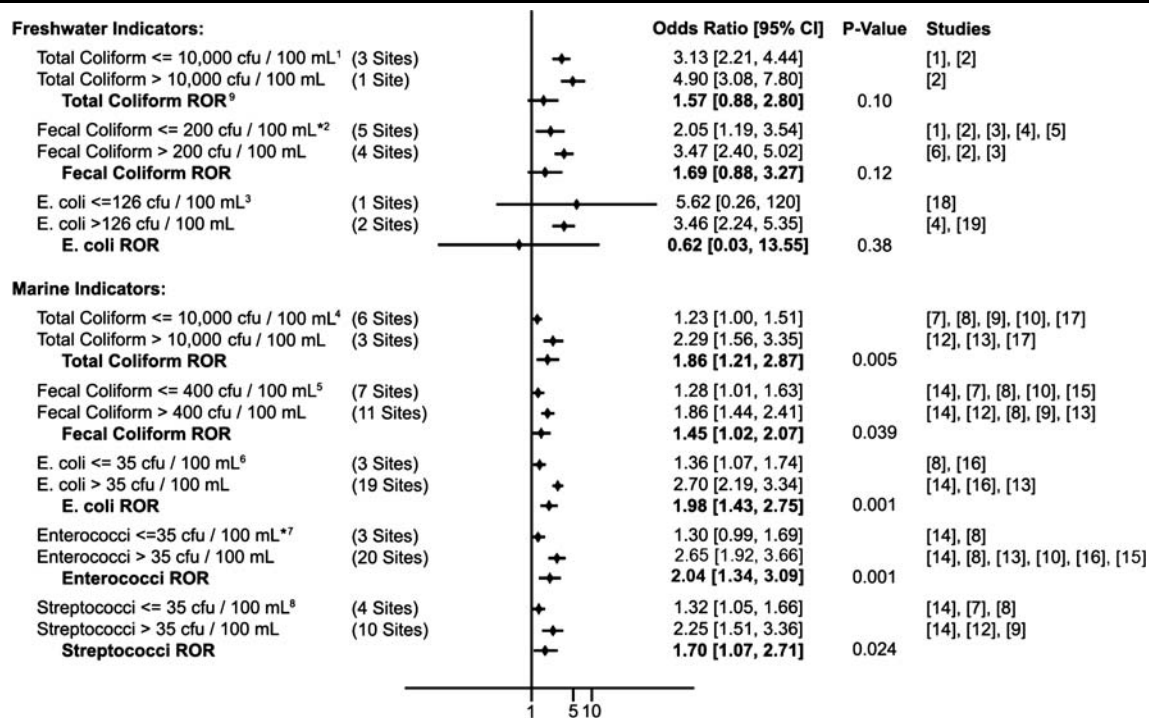
**Table 5** (Continued)

| Marine Indicator  | Study                        | Collection Method  | Lab Method  | Probable Source   | Study Groups  |
|-------------------|------------------------------|--|---|---|---|
| Fecal Coliform    | Cheung et al. (1990)         | 3 samples per beach, 1 m deep  | Membrane filtration, incubated on media                               | Human sewage discharge, stormdrains, livestock waste                          | Swimmers vs. Non-swimmers   |
|                   | Prieto et al. (2001)         | 30 cm below surface  | Standard Methods  | Sewage Systems  | Swimmers vs. Non-Swimmers   |
|                   | Jones et al. (1991)          | Sampled every 20 min at surf, 30 cm, chest depth, and 50 m off-shore | None Stated   | None Stated   | Bather vs. Non-bather Randomized                                    |
|                   | Cabelli et al. (1979)        | Sample several times per day, chest depth 4 in below surface         | Most Probable Number  | Sewage  | Swimmers vs. Non-swimmers   |
|                   | Alexander et al. (1992)      | 2 samples at waist depth   | Standard Methods  | Sewage  | Swimmers vs. Non-swimmers   |
|                   | Haile et al. (1999)          | Daily ankle depth samples  | Membrane Filtration   | Storm Drain Run-off   | Swimmers in more polluted water vs. swimmers in less polluted water |
|                   | Colford et al. (2007)        | Daily, hourly sampling   | Membrane Filtration and chromogenic substrate method                  | Non-point source, human contamination minimal                                 | Swimmers vs. Non-swimmers   |
|                   | Von Schirnding et al. (1992) | Day of trial, samples before and during trial                        | Standard membrane filtration methods                                  | Septic tank overflows, stormwater run-off, fecal contamination in river water | Swimmers vs. Non-swimmers   |
| <i>Klebsiella</i> | Cheung et al. (1990)         | 3 samples per beach, 1 m deep  | Membrane filtration, incubated on media                               | Human sewage discharge, stormdrains, livestock waste                          | Swimmers vs. Non-swimmers   |
|                   | Cabelli et al. (1979)        | Sample several times per day, chest depth 4 in below surface         | mC procedure  | Sewage  | Swimmers vs. Non-swimmers   |
| Staphylococci     | Cheung et al. (1990)         | 3 samples per beach, 1 m deep  | Membrane filtration, incubated on media                               | Human sewage discharge, stormdrains, livestock waste                          | Swimmers vs. Non-swimmers   |
|                   | Prieto et al. (2001)         | 30 cm below surface  | Standard Methods  | Sewage Systems  | Swimmers vs. Non-swimmers   |
|                   | Charoenca and Fujioka (1995) | None Stated  | Gelman membrane filtration, Vogel–Johnson Medium used with incubation | None Stated   | swimmers at polluted vs. less polluted                              |

indicator variables, with a “1” value indicating that the study adjusted for that covariate, and a “0” value for studies that did not adjust for that covariate.

For freshwater settings, the sources of heterogeneity for the fecal coliform meta-analysis were retrospective cohort study design (OR = 2.42, 1.08–5.41) and gender

(OR = 2.42, 0.76–6.61). These odds ratios can be interpreted as the single retrospective cohort study (Ferley et al. 1989) reported odds ratios that were 2.42 times greater than odds ratios reported from other study design types, and that studies that adjusted for gender reported odds ratios that were 2.42 times greater than odds



**Fig. 1** Summary of meta-analysis results, odds ratios, and Ratio of Odds Ratios (ROR). Number of individual sites with reported odds ratios is given next to each indicator, as well as the number of total studies included in each subanalysis in the Studies column. Footnotes: Meta-analysis summary results.

- total coliform cut-off: San Diego Water Board (2007)
- fecal coliform cut-off: California Department of Public Health (2000)
- E. coli* cut-off: U.S. EPA (1986)
- total coliform cut-off: California State Water Resources Control Board (1990)
- fecal coliform cut-off: California State Water Resources Control Board (1990)
- E. coli* cut-off: Haile et al. (1999)
- enterococcus cut-off: U.S. EPA (1986)
- streptococci cut-off: Ogan (1994)
- ROR is the ratio of odds ratios from high vs. low indicator settings

[1] Lee et al. (2002), [2] Ferley et al. (1989), [3] Fewtrell et al. (1992), [4] Medema et al. (1995), [5] Seyfried et al. (1985), [6] Dewailly et al. (1986), [7] Jones et al. (1991), [8] Cabelli et al. (1979), [9] Alexander et al. (1992), [10] Colford et al. (2007), [11] Wade et al. (2008), [12] Prieto et al. (2001), [13] Haile et al. (1999), [14] Cheung et al. (1990), [15] Von Schirnding et al. (1992), [16] Cabelli (1983), [17] Dwight et al. (2004), [18] Van Asperen et al. (1997), [19] Wiedenmann et al. (2006), [20] Charoenca and Fujioka (1995)

ratios reported from studies that did not adjust for gender. For fecal streptococcus, the main source of heterogeneity was study size (OR = 1.000041, 95% CI 0.99–1.00009).

For marine settings, the primary sources of heterogeneity in the meta-analysis considering *E. coli* were adjustment for visitor/native status of the study participants (OR = 1.80, 95% CI 1.13–2.88) and ethnicity (0.54, 95% CI 0.28–1.07). For enterococci, the main contributors to heterogeneity were adjustment for visitor/native status (OR = 2.10, 95% CI 1.09–4.06), exposure category below or above 35 cfu / 100 mL (OR = 1.38, 95% CI 0.84–2.27), gender (OR = 0.17, 95% CI 0.07–0.46), socioeconomic status (OR = 5.66, 95% CI 1.53–20.8), and age (OR = 0.36, 95% CI 0.20, 0.67).

## Publication bias

A statistical test for publication bias (Begg and Mazumdar 1994) suggested that for some marine indicators, publication bias may have been present (marine fecal streptococci = 0.001, marine fecal coliform  $p = 0.017$ , marine enterococci  $p = 0.001$ , marine *E. coli*  $p = 0.001$ , marine *Klebsiella*  $p = 0.003$ , marine *P. aeruginosa*  $p = 0.009$ , marine staphylococci  $p = 0.08$ ). The Begg test plots study effect size against a measure of the study's standard error or sample size, and determines if the study effect sizes are symmetrically distributed around the overall summary effect. If these plots are not symmetrically distributed, it is likely that publication bias may be present. This suggests that the summary relative risks reported in this study may be overestimates.



A further analysis was done using the “trim and fill” method proposed by Duval and Tweedie (2000), which non-parametrically attempts to account for the effects of publication bias and create an unbiased summary effect estimate (Duval and Tweedie 2000). For fecal streptococci in marine settings, publication bias was suspected in studies with indicator levels greater than 35 cfu / 100 mL. The “trim and fill” analysis gave a random effects OR of 1.97 (95% CI 1.37, 2.84) for studies with indicator levels greater than 35 cfu / 100 mL (previous unadjusted summary OR was 2.25, 95% CI 1.51–3.36). The ROR for marine fecal streptococci, adjusted for publication bias, becomes 1.49 (95% CI 0.97–2.30). For marine fecal coliforms, after adjusting for potential publication bias, the new ROR is 1.33 (95% CI 0.95, 1.88). For marine enterococci, the adjusted ROR was 1.31 (95% CI 0.86, 1.98). For marine *E. coli*, the ROR adjusted for publication bias was 1.76 (95% CI 1.22, 2.54). For marine *Klebsiella*, no ROR was calculated, but an adjusted summary OR was calculated to be 1.38 (95% CI 1.1, 1.74). Marine *P. aeruginosa* also had no ROR to adjust, but the adjusted OR was 1.36 (95% CI 1.12, 1.65). For marine staphylococci, the adjusted OR was 1.80 (95% CI 1.26, 2.56).

## Discussion

There are several microbiological indicators that are associated with skin-related health conditions in marine waters. This review has provided some evidence that skin-related health conditions are associated with exposure to contaminated recreational waters. All marine indicators showed statistically significant associations, with enterococci demonstrating the strongest association between bacterial levels and skin symptoms (ROR = 2.04, 95% CI 1.34–3.09). Cut-off points for freshwater indicators did not demonstrate statistically significant associations with skin-related outcomes, but were suggestive of an association. However, this review found that few published studies have examined indicator organisms and skin-related outcomes in freshwater situations. The small number of freshwater studies is probably an important factor in the lack of significant findings for freshwater indicators. For the freshwater analyses, the number of study sites per indicator ranged from a low of three to a high of nine sites. However, for marine studies, the minimum number of sites for any one indicator was nine sites, and the maximum was twenty.

For these indicators, predefined cut-off points were used. Other cut-off points may have been chosen that would have maximized the ROR, but such data exploration would have to be accounted for with penalized p-values for multiple comparisons. Additionally, looking cut-off points that would maximize the risk would be better answered with primary study data, rather than in a meta-analysis setting which suffers from more potential biases than individual studies.

Skin ailments (rashes, skin infections and irritation) among swimmers could arise from a wide variety of causes ranging from physical irritation to actual infection. However, since our review observed a higher rate of skin ailments at marine sites with higher levels of fecal contamination, a cause independent of physical irritation is implied. Skin ailments among swimmers may be caused by a wide variety of pathogenic microorganisms, some of which would be naturally occurring and not necessarily expected to be associated with fecal indicator bacteria (cyanobacteria, cercarial dermatitis, sea-bather's eruption caused by zooplankton) (Burke 2002). However, other pathogens such as *Pseudomonas*, *Staphylococcus*, and adenovirus that could cause skin irritations could co-occur with fecal indicators associated with run-off, sewage discharge or through the shedding of other swimmers (CDC 2008).

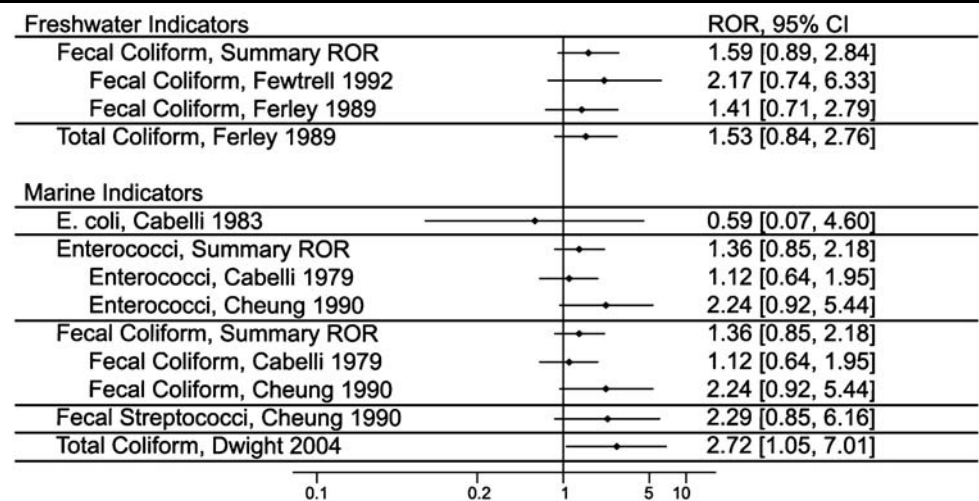
The meta-regressions provided interesting information that could prove valuable for future studies in recreational water. The results from the meta-regressions indicate that there is evidence that controlling for native or visitor status of study participants may be an important factor to consider in future studies. The marine studies that used *E. coli* and adjusted for visitor/native status reported an odds ratio that was 1.80 times greater compared to studies that did not adjust (95% CI 1.13–2.88), and studies that adjusted for ethnicity had odds ratios that were 0.54 times smaller than studies that did not (95% CI 0.28–1.07). Thus, both native/visitor status and ethnicity appear to be important covariates to consider for adjustment. Studies of enterococci also supported the finding that visitor/native status was an important variable to adjust for (OR = 2.10, 95% CI 1.09–4.06), but other explanations of heterogeneity included exposure category below or above 35 cfu / 100 mL (OR = 1.38, 95% CI 0.84–2.27), gender (OR = 0.17, 95% CI 0.07–0.46), socioeconomic status (OR = 5.66, 95% CI 1.53–20.8), and age (OR = 0.36, 95% CI 0.20, 0.67).

Other possible sources of heterogeneity are indicated in the freshwater meta-analyses. Among studies that examined fecal coliforms as an indicator, the single retrospective cohort study (Ferley et al. 1989) reported an odds ratio that was 2.42 times greater than studies that did not use the retrospective cohort design (95% CI 1.08–5.41). For studies examining fecal streptococcus, it appeared that larger studies tended to report larger odds ratios. For a 1,000-person increase in study size, the odds ratio increased by a factor of 1.04 times (95% CI 0.99–1.09, p-value 0.08).

## Biases

Publication bias was also seen in several of the subanalyses. Analysis of marine indicators indicated that with the exception of total coliforms, publication bias was present for the rest of the indicators. For fecal streptococci, fecal coliforms, and marine enterococci, after adjusting for publication bias

**Fig. 2** Studies with internal control groups (OR comparing swimmers to non-swimmers in water with lower than recommended indicator levels versus OR comparing swimmers to non-swimmers in water with higher than recommended indicator levels). Each study has a ROR reported, and if multiple studies are present for a given indicator, the RORs from each individual study are meta-analyzed into a summary ROR



with the trim and fill method, the summary RORs changed from significant findings to non-significant findings. However, the ROR for marine *E. coli* remained significant. While this might cast doubt on the usefulness of fecal streptococci, fecal coliforms, and enterococci as indicator organisms, the direction of the ROR still indicates an association between indicator concentration and risk of skin conditions in bathers. However, these findings reinforce the idea that publication bias tends to overstate the association between indicator concentrations and the risk of skin disease.

Another source of bias was reported by (Fleisher and Kay 2006). It was found that bathers who perceived that there was a health risk associated with bathing in marine waters reported significantly higher rates of skin ailments compared to bathers who did not recognize any health risk associated with bathing in marine waters. Only one study in this systematic review adjusted for this variable (Haile et al. 1999). Thus, there is the potential for participants in other studies to have over-reported their incidence of skin ailments, thus theoretically causing results in those studies to be biased upwards.

Another potential source of bias is the comparison of swimmers to non-swimmers. These populations may have inherent differences that might confound the association between indicators and skin-related outcomes. For example, swimmers might be healthier individuals while non-swimmers were more prone to illness, or perhaps individuals with higher SES might be better educated about the risks associated with swimming, while those with lower SES might be more willing to swim and become exposed. Also, swimmers might be more likely to report symptoms than non-swimmers because they suspected that swimming may have caused whatever symptoms they experienced.

Yet another potential source of bias is that some studies relied on individuals to self-report their exposure and outcome status after the study. Swimmers might have poor recall of their exact exposure status, and they may have been more likely to report symptoms if they knew they had

been exposed for long periods of time. This form of recall bias may have been present in many studies, because few were able to assign defined swimming activities and times to study participants or to employ physicians to assess outcome status in a blinded fashion.

In order to minimize biases associated with comparing disparate study populations, another analysis was conducted calculating ROR measures for studies with internal controls (an OR for high indicator concentration swimmers vs. non-swimmers and an OR for low indicator concentration swimmer vs. non-swimmers). Nine out of ten studies with internal controls demonstrated an elevated odds ratio for skin-associated outcomes in more polluted waters compared to less polluted waters, though only one was statistically significant (Fig. 2).

An alternative way to deal with the biases present in various studies is to assign different weights to different studies, with more rigorous and high quality studies receiving more weight while smaller and potentially more biased studies receiving lower weights. While weighting schemes were considered, the method of assigning weights is very subjective. Without a standard, systematic method of assigning weights, the results of this study might be skewed to indicate that a certain indicator was worse or better than the raw data suggests. Rather than weight the data, the authors chose to allow the readers to look at the data themselves and draw their own conclusions.

#### Suggested further research

It is evident that the current state of the freshwater indicator literature with respect to skin-related health outcomes is lacking. Future studies should continue to consider skin-associated outcomes using both traditional and novel indicators of recreational water quality. Another issue that should be explored would be for studies to use a measure of bather density and determine if it has any influence on health re-

| Freshwater Indicators:                |            | Indicator Concentration (cfu / 100 mL) |        |             |
|---------------------------------------|------------|--|--------|-------------|
|                                       |            | Mean                                   | Median | Range       |
| Total Coliform <= 10,000 cfu / 100 mL | (3 Sites)  | 1079                                   | 786    | 10-2440     |
| Total Coliform > 10,000 cfu / 100 mL  | (1 Site)   | 2446                                   | 24461  | 24461-24461 |
| Fecal Coliform <= 200 cfu / 100 mL    | (5 Sites)  | 69                                     | 76     | 6-133       |
| Fecal Coliform > 200 cfu / 100 mL     | (4 Sites)  | 889                                    | 762    | 285-1749    |
| <i>E. coli</i> <=126 cfu / 100 mL     | (1 Sites)  | 68                                     | 68     | 68-68       |
| <i>E. coli</i> >126 cfu / 100 mL      | (2 Sites)  | 153                                    | 153    | 136-170     |
| Enterococcus >33 cfu / 100 mL         | (3 Sites)  | 297                                    | 83     | 37-770      |
| Staphylococci (n/a cut-point)         | (4 Sites)  | 45                                     | 13     | 3-151       |
| Streptococci (n/a cut-point)          | (7 Sites)  | 31                                     | 15     | 13-82       |
| <b>Marine Indicators:</b>             |            |  |        |             |
| Total Coliform <= 10,000 cfu / 100 mL | (6 Sites)  | 744                                    | 574    | 37-2022     |
| Total Coliform > 10,000 cfu / 100 mL  | (3 Sites)  | 10667                                  | 10000  | 10000-12000 |
| Fecal Coliform <= 400 cfu / 100 mL    | (7 Sites)  | 95                                     | 77     | 8-254       |
| Fecal Coliform > 400 cfu / 100 mL     | (11 Sites) | 797                                    | 565    | 400-3166    |
| <i>E. coli</i> <= 35 cfu / 100 mL     | (3 Sites)  | 11                                     | 15     | 2-15        |
| <i>E. coli</i> > 35 cfu / 100 mL      | (19 Sites) | 1311                                   | 269    | 35-10400    |
| Enterococci <=35 cfu / 100 mL         | (4 Sites)  | 22                                     | 28     | 7-31        |
| Enterococci > 35 cfu / 100 mL         | (21 Sites) | 1250                                   | 168    | 35-9160     |
| Streptococci <= 35 cfu / 100 mL       | (4 Sites)  | 21                                     | 24     | 4-32        |
| Streptococci > 35 cfu / 100 mL        | (10 Sites) | 159                                    | 101    | 40-500      |
| <i>Klebsiella</i> (n/a cut-point)     | (11 Sites) | 205                                    | 105    | 4-943       |
| <i>P. aeruginosa</i> (n/a cut-point)  | (13 Sites) | 11                                     | 5      | 0.07-46     |
| Staphylococci (n/a cut-point)         | (11 Sites) | 952                                    | 921    | 100-2963    |

**Fig. 3** Microbial indicator concentrations by indicator. Mean, median, and minimum/maximum values for each microbial indicator are reported

lated outcomes. Bather density could be an important variable because higher bather densities might elevate the concentration of bacteria in the water by re-suspending sediments or shedding of indicators and/or pathogens.

### Limitations

One of the major criticisms of meta-analyses of observational studies is that it is probable that there are biases and confounding factors that have not been adjusted for in the individual studies, and that the populations in each study are not comparable to populations in other studies (Shapiro 1994). This would make any summary measures suspect. In order to attempt to deal with the heterogeneity of the data, random-effects analyses were used whenever appropriate. There was also the possible bias that studies without significant findings may not have been published. Although every effort was made to obtain relevant studies, dissertations, and reports, some studies may not have been found, and some studies that were relevant may have not published enough data to extract because no significant findings were found.

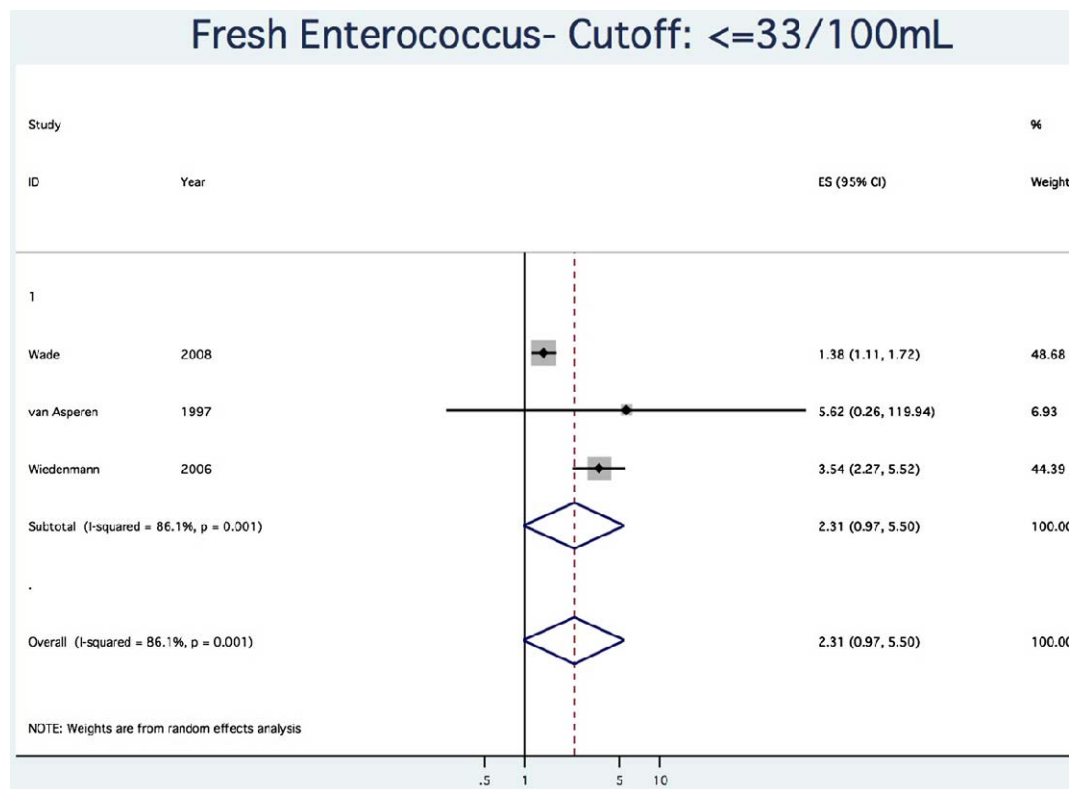
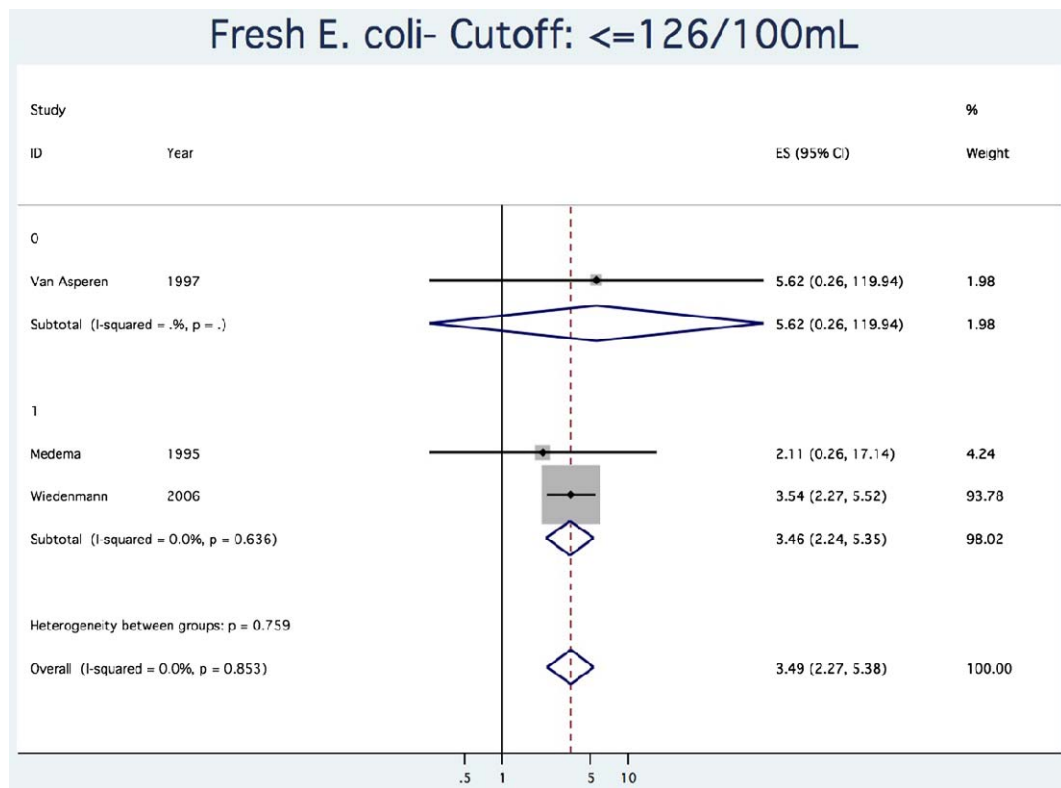
Another limitation to consider is the vast difference between many of the study populations and sites. The studies included range across Asia (Lee et al. 2002; Cheung et

al. 1990), Europe (Jones et al. 1991; Alexander et al. 1992; Fewtrell et al. 1992; Ferley et al. 1989; Medema et al. 1995; Prieto et al. 2001), Africa (Von Schirnding et al. 1992) and North America (Cabelli et al. 1979; Cabelli 1983; Seyfried et al. 1985; Dewailly et al. 1986; Haile et al. 1999; Dwight et al. 2004; Colford et al. 2007). Some studies specifically looked for tourists (Cabelli 1983) while other studies dealt with more native populations (Dwight et al. 2004).

### Conclusions

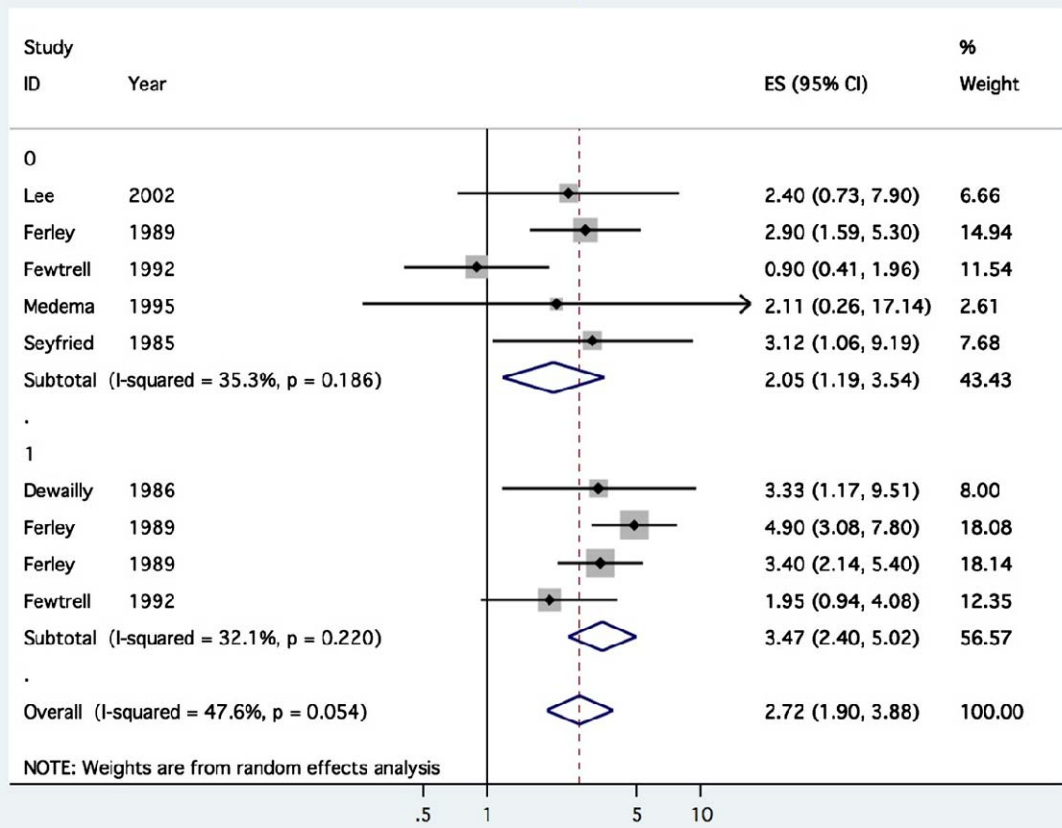
The results of this review indicate that skin complaints may be significantly more likely to occur among swimmers exposed to marine waters with measured levels of total coliform, fecal coliform, *E. coli*, enterococci, and streptococci above the recommended cut-off points for these indicator organisms. No statistically significant results were found for freshwater cut-off points.

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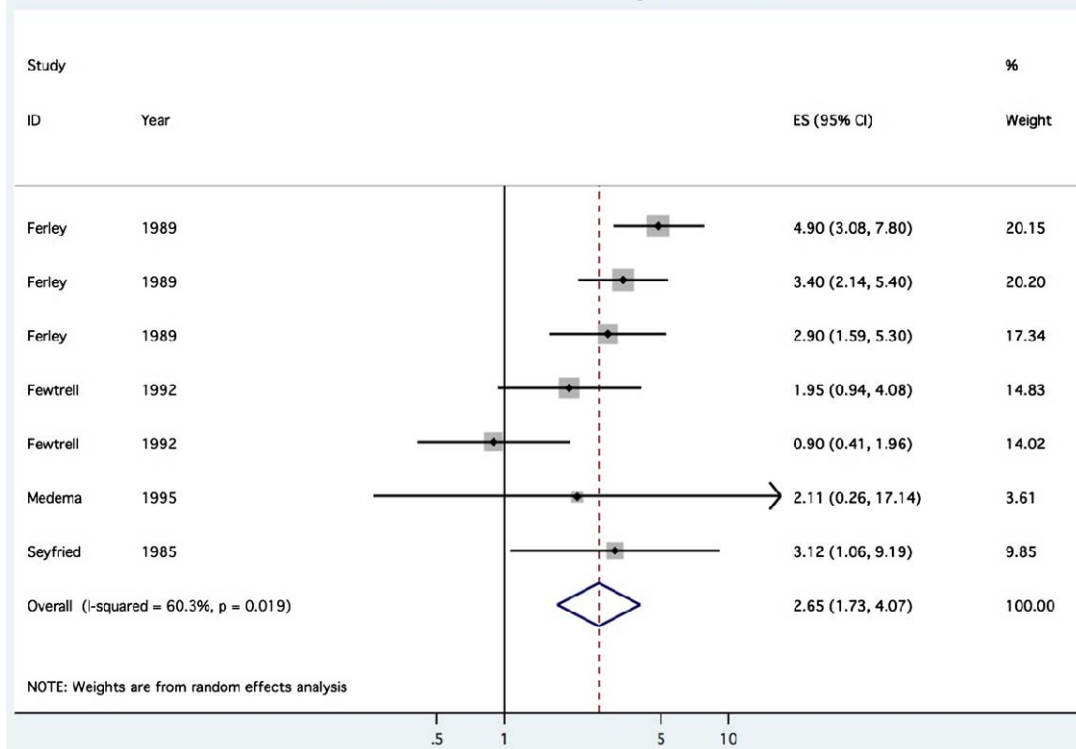




## Fresh Fecal Coliform- Cutpoint: $\leq 200/100\text{mL}$

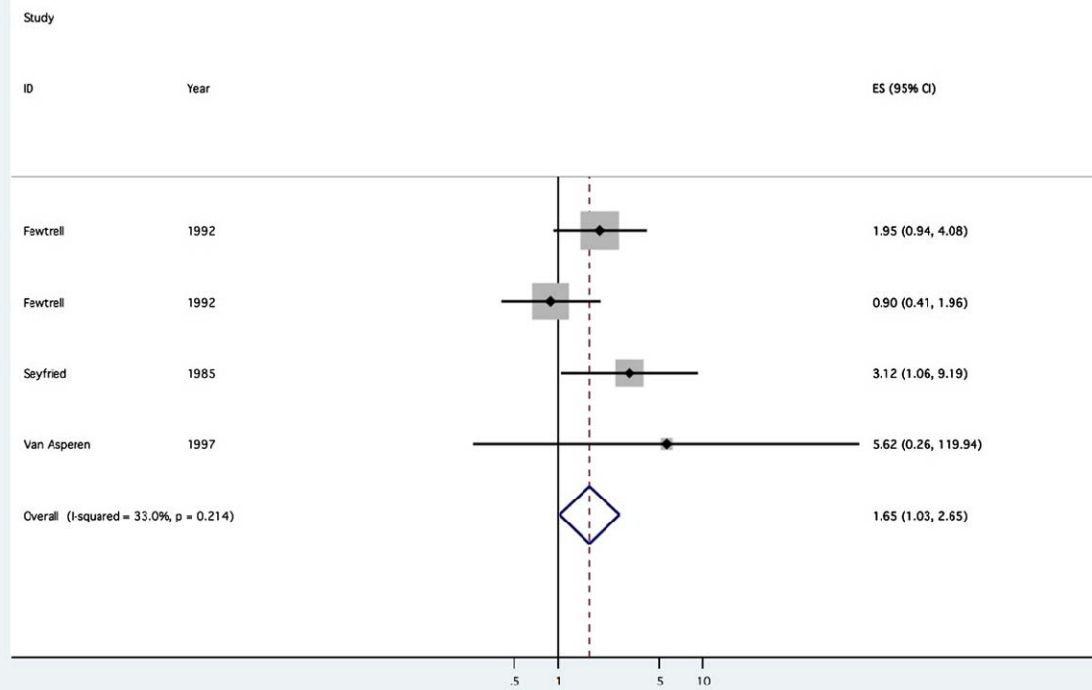


## Fresh Fecal Streptococci

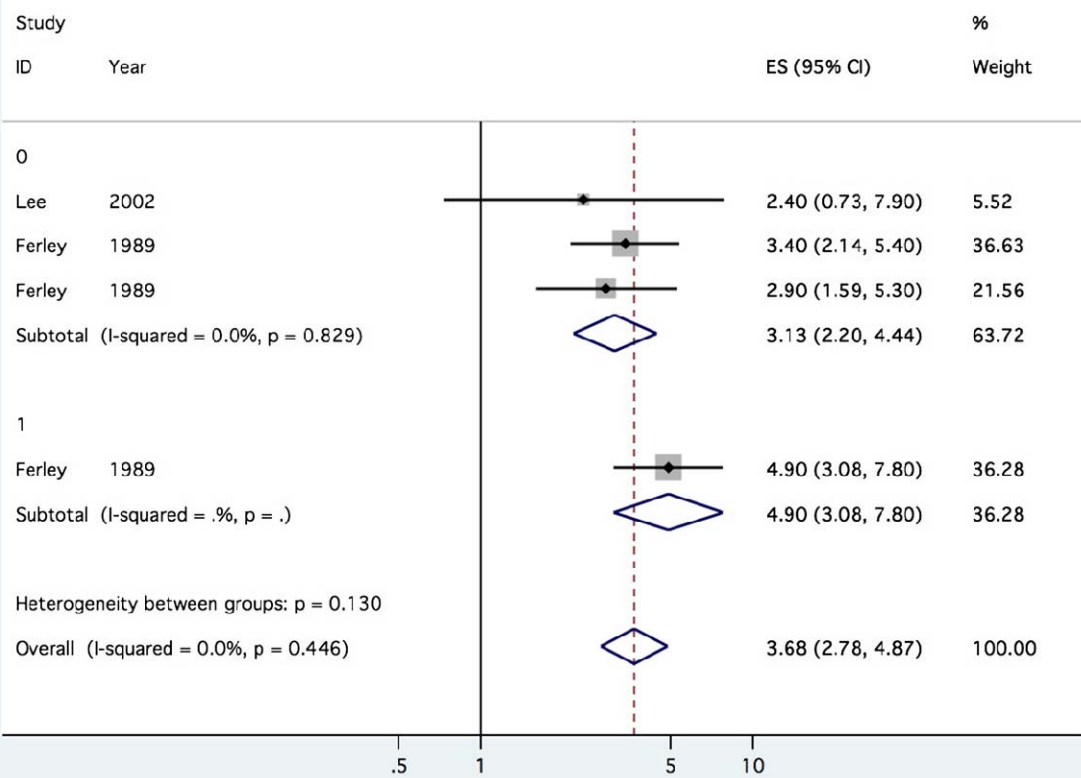




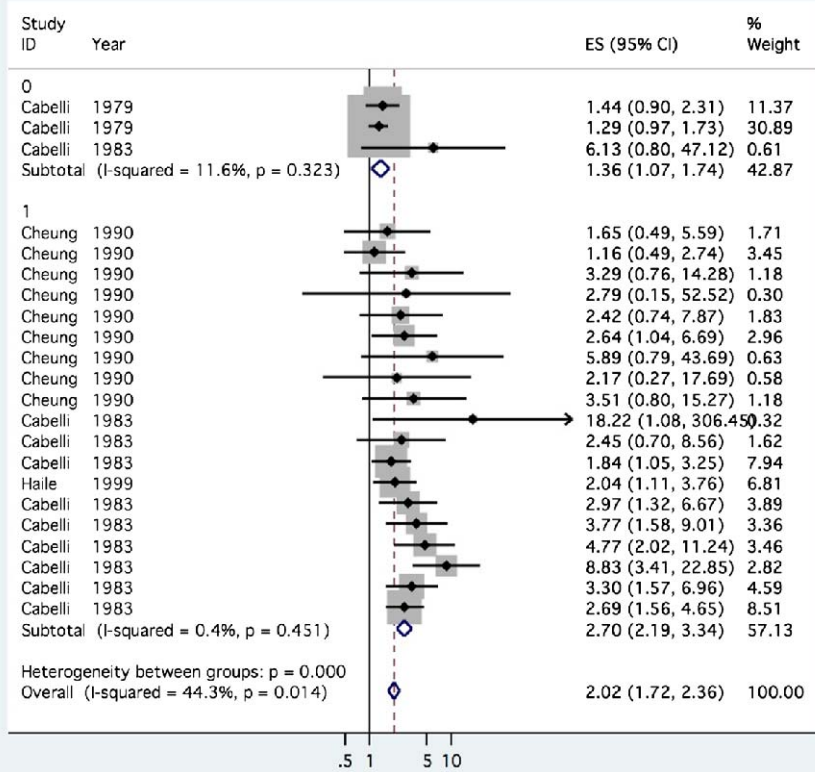
## Fresh Staphylococci



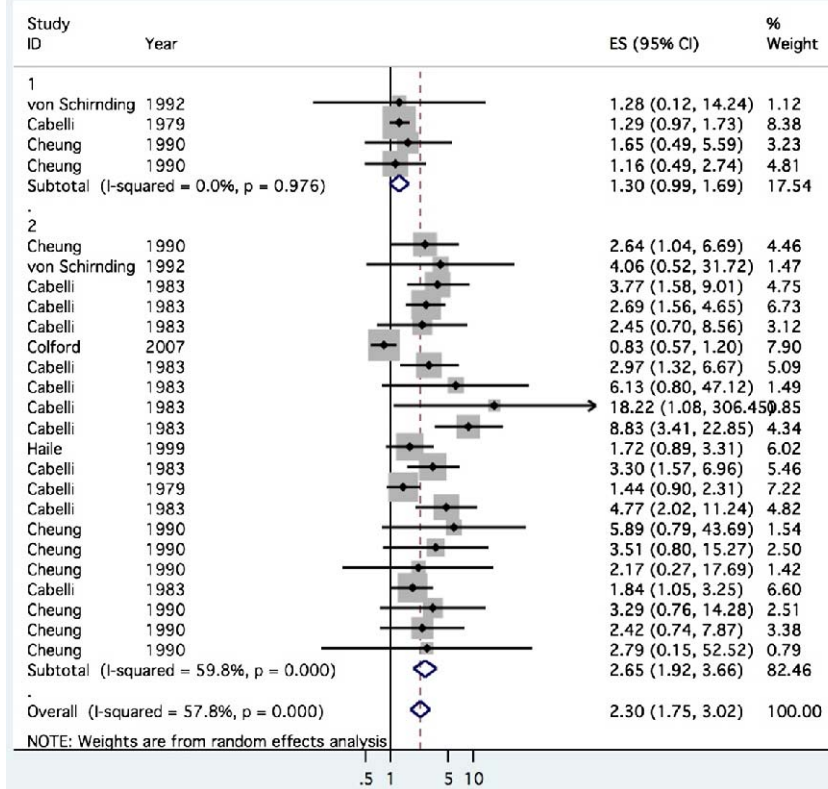
## Fresh Total Coliform- Cutoff: $\leq 10000/100\text{mL}$



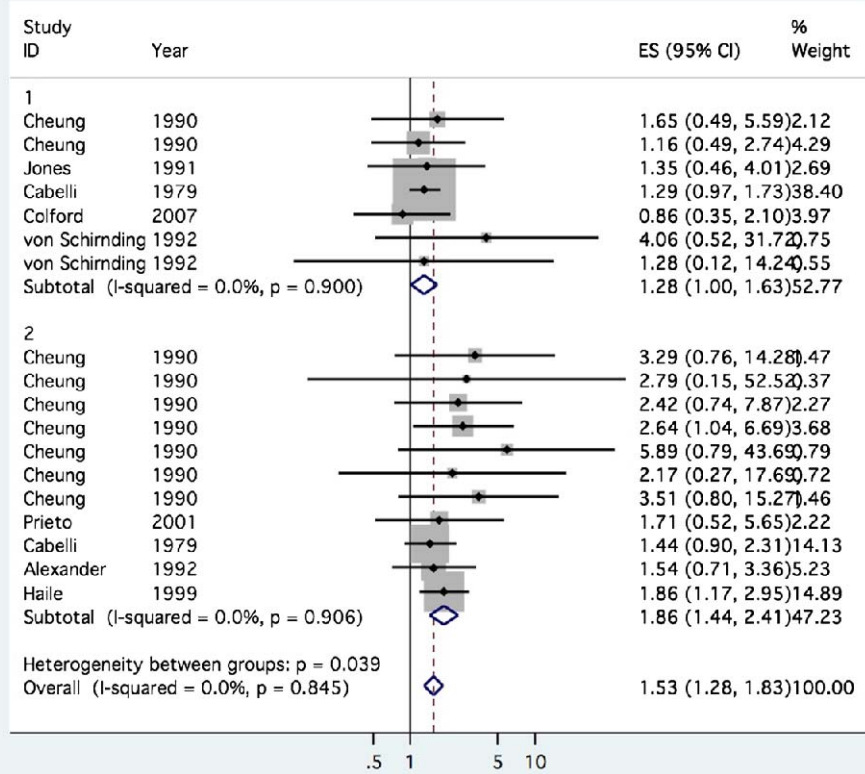
## Marine E. coli- Cutoff: $\leq 35/100$ mL



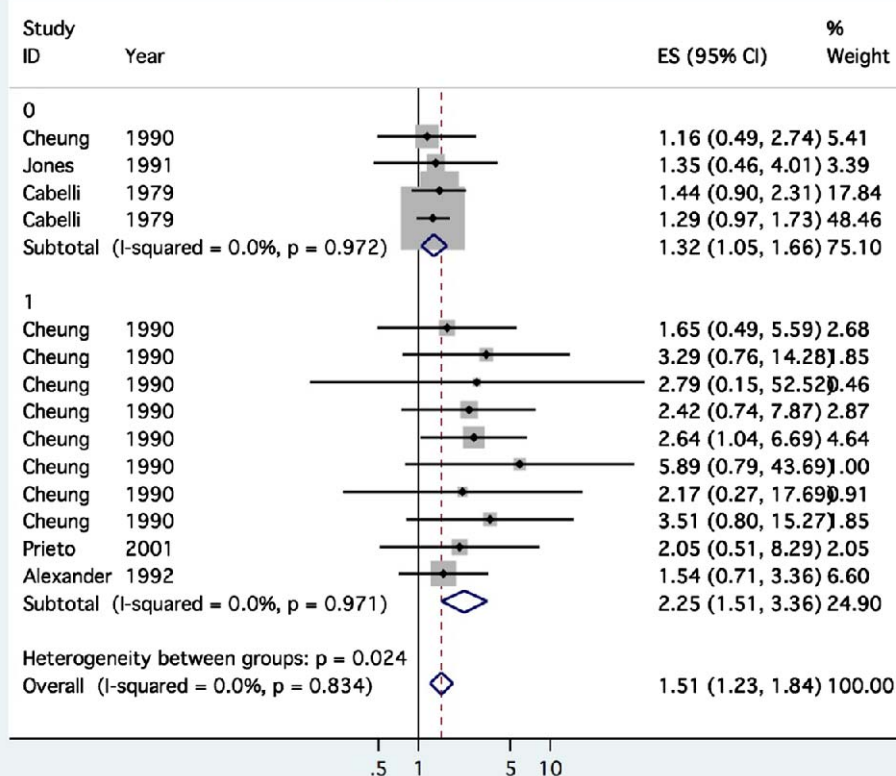
## Marine Enterococci- Cutoff: $\leq 35/100$ mL



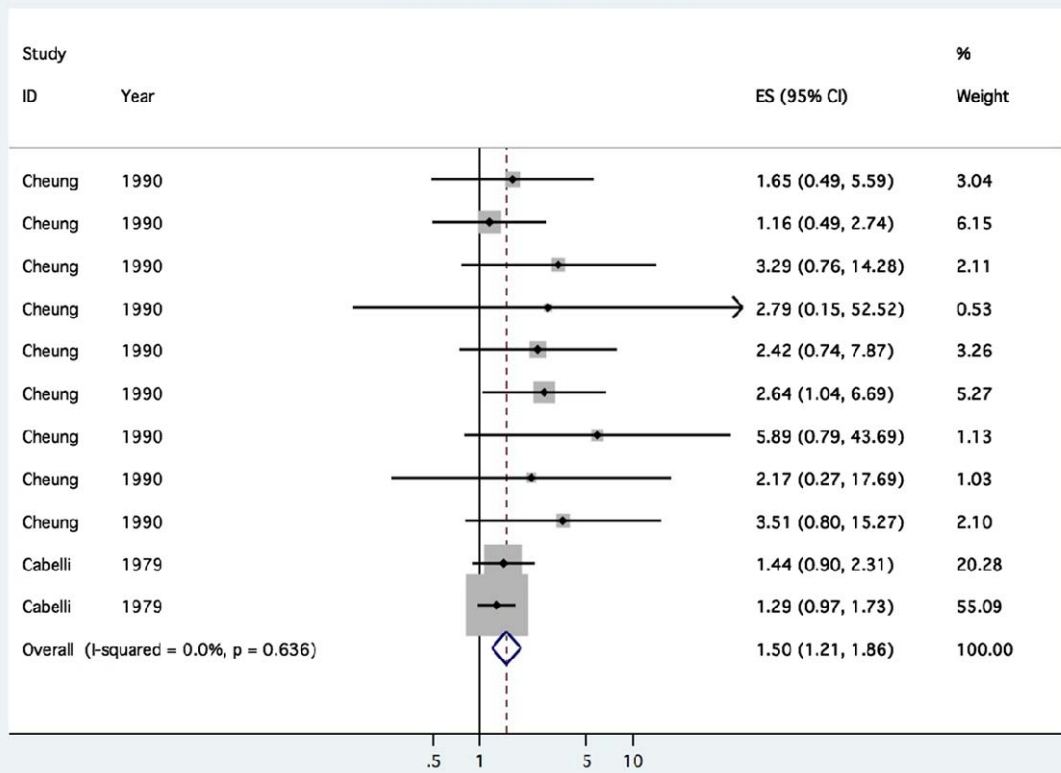
## Marine Fecal Coliforms- Cutoff: $\leq 400/100$ mL



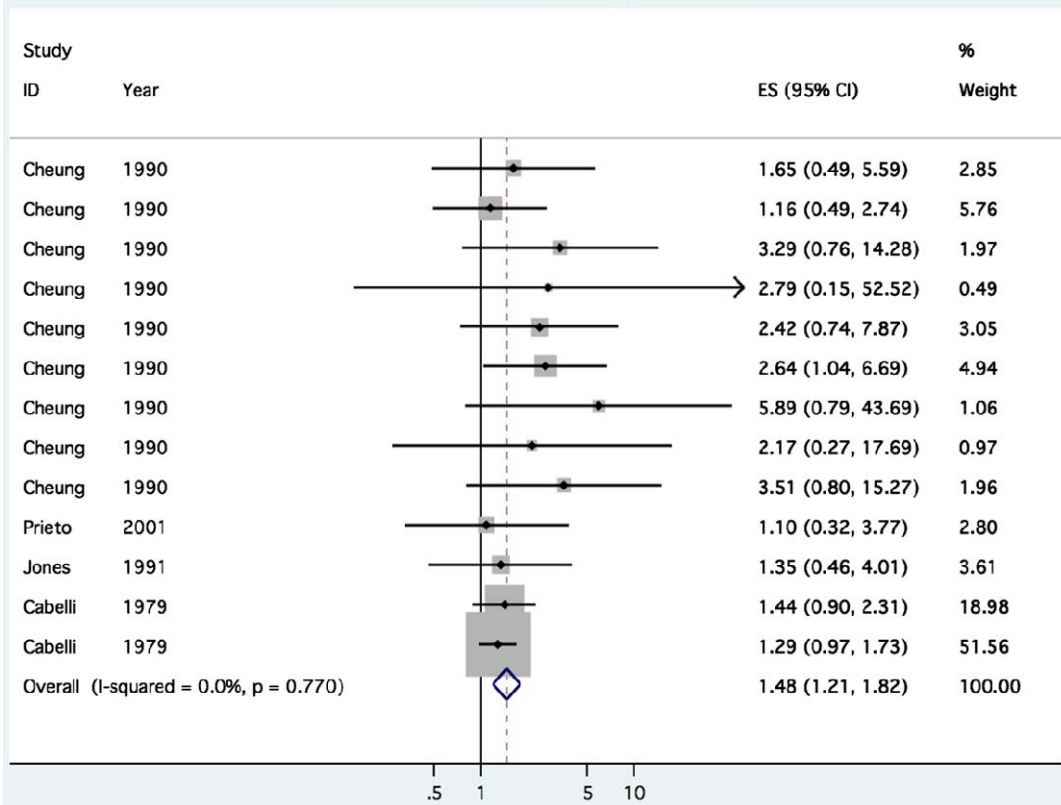
## Marine Fecal Strep- Cutoff: $\leq 35/100$ mL



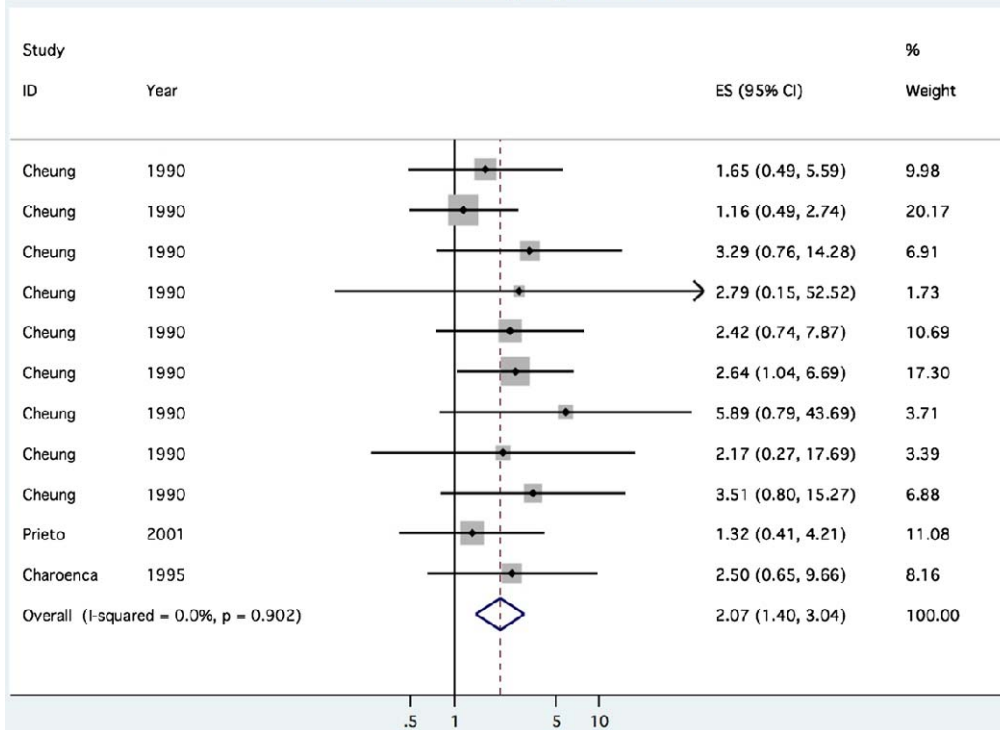
## Marine Klebsiella



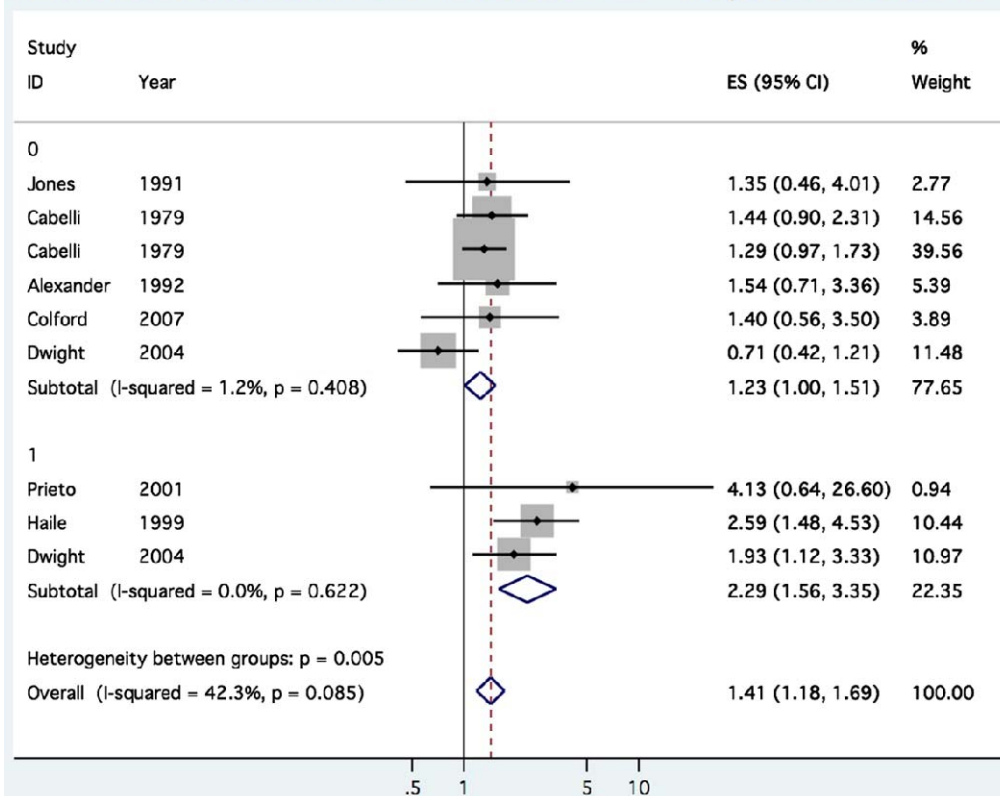
## Marine P. aeruginosa



## Marine Staphylococci



## Marine Total Coliform- Cutoff: $\leq 10,000/100$ mL





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